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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,637	06/01/2006	Ryuji Ueno	Q76459	8742

23373 7590 01/06/2011

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
01/06/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/562,637	UENO, RYUJI	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-16 and 18-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-16 and 18-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/20/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response, Amendment and Applicant's Arguments/Remarks filed 10/25/10 and the Information Disclosure Statement (IDS) filed 12/20/10 is acknowledged.

Applicant has overcome the following objections/rejections by virtue of the amendment to the claims and/or persuasive remarks: (1) The claim objection for claim 1 has been withdrawn; (2) The 35 U.S.C. 102(e) rejection of claims 1 and 4 over Ueno et al. (U.S. Pat. No. 6,583,174) has been withdrawn; (3) The 35 U.S.C. 102(e) rejection of claims 1 and 4 over Ueno et al. (EP 0979651) has been withdrawn and (4) The 35 U.S.C. 102(e) rejection of claims 1-19 over Ueno et al. (WO 03/030912) has been withdrawn.

Claims 1, 6-16 and 18-28 are pending in this action. Claims 1, 6-16 and 18-19 have been amended. New claims 20-28 have been added. Claims 2-5 and 17 have been cancelled. Claims 1, 6-16 and 18-28 remain rejected.

* * * * *

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 20 December 2010 was filed after the mailing date of the Non-Final Office Action on 06/25/10. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 6-16 and 18-21, 24, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (hereinafter "Ueno") (U.S. Pat. No. 6,583,174).

Ueno teaches a composition comprising a bicyclic compound and a glyceride compound and a method for stabilizing the bicyclic compound comprising the step of admixing the same with a glyceride (column 1, line 9 - col. 3, line 36). In one embodiment, the composition may comprise the bicyclic compound of formula (III), glyceride and an enteric coating in which the bi-cyclic compound is present in a ratio of at least 1:1, especially, 20:1 with respect to its tautomeric monocyclic compound. The composition may be formulated as capsule and outer surface of the capsule may be coated by the enteric coating, or enteric materials may be compounded into the capsule base (col. 21, line 21 – col. 22, line 47).

The compound of formula (III) may be provided as solid product comprising substantially no monocylic tautomer of the same and the present invention also covers a composition comprising the compound of formula (III) and a enteric coating, wherein the composition comprises substantially no monocyclic tautomer of the compound (col. 4, line 60 – col. 5, lines 1-32).

The compositions and formulas provided by Ueno read on the limitations of instant claims 5-19. The teachings of Ueno amply demonstrate that it would be prima facie obvious to utilize any bicyclic prostaglandin compounds provided in an oral formulation in combination with a glyceride with the expected result of obtaining improved pharmaceutical activity and stability. The reference is clearly suggestive of a composition comprising a bicyclic prostaglandin whereby the active agent can be provided either as a mixture with the enteric coating or alternatively the enteric coating can be supplied as a coating for the outer surface of the dosage form (i.e., capsule).

With regards to the instant "enteric" coating, it is noted that Ueno does not explicitly teach "enteric" coatings but rather teaches general "coatings" and "capsulating agents" at col. 22, line 31. However the teaching of the generic "coatings and capsulating agents" by Ueno would encompass the species of "enteric" coatings claimed by Applicant. The general disclosure of "coatings and capsulating agents" by Ueno is therefore sufficient to read on the "enteric" coating claimed by Applicant. Ueno expressly teaches that coatings and capsulating agents can be employed in compositions intended for oral administration and as a result, would render obvious, the "enteric" coating feature recited herein by Applicant, as such coatings/capsulating agents would include "enteric" coatings.

This rejection is maintained and applied to newly added claims 20, 21, 24, 25, 27 and 28.

With regards to Applicant's limitations of new claims 20, 21, 24 and 25 that the "composition exhibits reduced nausea inducing effect than that of a composition without the enteric coating", it is the position of the Examiner that this limitation is met by Ueno. Ueno discloses the use of coatings and capsulating agents and thus, one of ordinary skill in the art would reasonably conclude that the nausea-induced effect would be reduced based on the incorporation of the coatings/capsulating agents of Ueno.

With regards to Applicant's limitations of new claims 27 and 28 of "for preventing irritation of the upper gastric organs" of instant claim 27 and of "for improving pharmaceutical effect of the bicyclic compound to the living body" of instant claim 28, these limitations are met by Ueno. Ueno, as delineated above, discloses the use of coatings and capsulating agents and thus, one of ordinary skill in the art would reasonably conclude that irritation of gastric organs would be reduced and/or eliminated based on the incorporation of the coatings/capsulating agents of Ueno. Furthermore, the pharmaceutical effect of the bicylic compound would be improved based on the coatings/capsulating agents of Ueno, absent a showing of evidence to the contrary.

The instant invention would have been prima facie obvious to one of ordinary skill in the art, given the teachings of Ueno ('174) discussed above.

* * * * *

Claims 1, 6-16 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (hereinafter "Ueno") (EP 0979651).

Ueno ('651) teaches an anti-portal hypertensive agent comprising a 15-keto-prostaglandin compound as an active ingredient (Abstract). The composition is administered by oral administration (page 6, lines 7-15). Examples of solid compositions include tablets and pills that may be coated with an enteric coating or gastroenteric film (p. 6, lines 26-34). The formulas and compositions of the present invention are encompassed by Ueno, who discloses various prostaglandin compounds of the present invention. Thus, the compositions and formulas provided by Ueno read on the limitations of instant claims 5-19. The teachings of Ueno amply demonstrate that it would be prima facie obvious to utilize any prostaglandin compounds provided in an oral formulation in combination with application of enteric coatings in order to effectively treat portal hypertension.

With regards to the instant "enteric" coating, Ueno teaches that their "tablets or pills may be gastric or enteric-coated preparations" ([0060]). Ueno '651 is directed to enteric-coated preparations and thus is sufficient to meet the instant claims. One of ordinary skill in the art would be amply motivated to apply the enteric coatings of Ueno for release of drug (i.e., bicyclic compounds) into the intestines based on Ueno's teaching that enteric coatings can be employed.

This rejection is maintained and applied to newly added claims 20-28.

With regards to Applicant's limitations of new claims 20, 21, 24 and 25 that the "composition exhibits reduced nausea inducing effect than that of a composition without the enteric coating", it is the position of the Examiner that this limitation is met by Ueno. Ueno discloses the administration of enterically-coated tablets or pills. Thus, one of ordinary skill in the art would reasonably conclude that nausea would necessarily be prevented and/or that the

nausea-induced effect would be reduced based on the incorporation of the enteric coating applied on the compound.

With regards to Applicant's limitations of new claims 22, 23 and 26 for the specific enteric coatings, Ueno teaches that their "tablets or pills may be enteric-coated preparations" ([0060]). While the specific coatings are not disclosed, one of ordinary skill in the art would employ any specific enteric coating, based on personal preference and/or the intended outcome. Ueno '651 is directed to enteric-coated preparations, whereby sustained release of the active ingredient is obtained; and thus, the particular enteric coating employed does not impart a patentable distinction over the teachings of Ueno, who explicitly recognizes and teaches use of enteric coatings.

With regards to Applicant's limitations of new claims 27 and 28 of "for preventing irritation of the upper gastric organs" of instant claim 27 and of "for improving pharmaceutical effect of the bicyclic compound to the living body" of instant claim 28, these limitations are met by Ueno. Ueno, as delineated above, discloses the use of enteric coatings and thus, one of ordinary skill in the art would reasonably conclude that irritation of gastric organs would be reduced and/or eliminated based on the incorporation of the enteric coatings of Ueno. Ueno expressly teaches the use of enteric-coatings and consequently, would be effective in preventing irritation and/or nausea to a subject. Furthermore, the pharmaceutical effect of the bicylic compound would be improved based on the enteric coatings of Ueno, absent a showing of evidence to the contrary.

The instant invention would have been prima facie obvious to one of ordinary skill in the art, given the teachings of Ueno ('651) discussed above.

* * * * *

Claims 1, 6-16 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (hereinafter "Ueno") (WO 03/030912).

Ueno ('912) teaches a prostaglandin compound as a chloride channel opener (Abstract). The composition is administered by oral administration (page 23, lines 10-19). Examples of solid compositions include tablets and pills that may be coated with an enteric coating or gastroenteric film (p. 25, lines 5-21). The formulas and compositions disclosed in instant claims 6-16, 18 and 19 are encompassed and disclosed by Ueno, who discloses various prostaglandin compounds of the present invention.

With regards to the instant "enteric" coating, Ueno teaches that their "tablets or pills may be gastric or enteric-coated preparations" (page 25, lines 12-13). Ueno '912 is directed to enteric-coated preparations and thus is sufficient to meet the instant claims. One of ordinary skill in the art would be amply motivated to apply the enteric coatings of Ueno for release of drug (i.e., bicyclic compounds) into the intestines based on Ueno's teaching that enteric coatings can be employed.

This rejection is maintained and applied to newly added claims 20-28.

With regards to Applicant's limitations of new claims 20, 21, 24 and 25 that the "composition exhibits reduced nausea inducing effect than that of a composition without the enteric coating", it is the position of the Examiner that this limitation is met by Ueno. Ueno discloses the administration of enterically-coated tablets or pills. Thus, one of ordinary skill in the art would reasonably conclude that nausea would necessarily be prevented and/or that the

nausea-induced effect would be reduced based on the incorporation of the enteric coating applied on the compound.

With regards to Applicant's limitations of new claims 22, 23 and 26 for the specific enteric coatings, Ueno teaches that their "tablets or pills may be enteric-coated preparations" ([0060]). While the specific coatings are not disclosed, one of ordinary skill in the art would employ any specific enteric coating, based on personal preference and/or the intended outcome. Ueno '912 is directed to enteric-coated preparations, whereby sustained release of the active ingredient is obtained; and thus, the particular enteric coating employed does not impart a patentable distinction over the teachings of Ueno, who explicitly recognizes and teaches use of enteric coatings.

With regards to Applicant's limitations of new claims 27 and 28 of "for preventing irritation of the upper gastric organs" of instant claim 27 and of "for improving pharmaceutical effect of the bicyclic compound to the living body" of instant claim 28, these limitations are met by Ueno. Ueno, as delineated above, discloses the use of enteric coatings and thus, one of ordinary skill in the art would reasonably conclude that irritation of gastric organs would be reduced and/or eliminated based on the incorporation of the enteric coatings of Ueno. Ueno expressly teaches the use of enteric-coatings and consequently, would be effective in preventing irritation and/or nausea to a subject. Furthermore, the pharmaceutical effect of the bicylic compound would be improved based on the enteric coatings of Ueno, absent a showing of evidence to the contrary.

The instant invention would have been prima facie obvious to one of ordinary skill in the art, given the teachings of Ueno ('912) discussed above.

* * * * *

Response to Arguments

Applicant's arguments filed 25 October 2010 have been fully considered and were found to be partially persuasive.

- **Claim Objection:**

Applicant stated, "Applicants have made the grammatical correction as indicated by the Examiner for the objection to claim 1".

This argument was persuasive by virtue of the amendment to claim 1. Accordingly, the claim objection has been withdrawn.

- **Rejection under 35 U.S.C. §102(e) over Ueno (US'174):**

Applicant argued, "There is no disclosure of an enteric coating or enteric materials that may be compounded into the capsule base, either in the particular disclosure cited by the Examiner or elsewhere in the patent. Rather, Ueno '174 only generally discloses coatings and capsulating agents at col. 22, line 31, and Applicant submits that such a general disclosure does not teach or suggest the enteric requirement of the present invention in particular."

Applicant's arguments have been considered and were found persuasive. Accordingly, the 35 U.S.C. 102(e) rejection of claims 1 and 4 over Ueno et al. (U.S. Pat. No. 6,583,174) has been withdrawn.

- **Rejection under 35 U.S.C. §102(e) over Ueno (EP'651)**:

Applicant argued, "Applicant notes initially that this rejection is improper because Ueno '651 is not 35 U.S.C. 102(e) prior art, since it is not a U.S. patent, a U.S. published patent application, or a WO publication that designated the U.S. and was published in English. Accordingly, this 35 U.S.C. 102(e) rejection should be withdrawn.

Further, Applicant notes that while Ueno '651 generally discloses an enteric-coated preparation at page 6, line 29, it does not teach or suggest particular coatings such as those set forth in the disclosure beginning at page 22, line 11 in the present application.

In addition, Applicant notes that Ueno '651 describes "Tablets or pills may be gastric or enteric-coated preparation" (see [0060] of Ueno '651).

Applicant submits that Ueno '651 does not describe or suggest that nausea in the subject is effectively prevented by administering the specific bicyclic compound as an enteric coated formulation to a subject, and the bicyclic tautomer is well protected even under an acidic condition by providing said compound with an enteric coating (see page 20, lines 4-16 of the present application). In addition, Ueno '651 does not describe or suggest which is a more suitable formulation for the bicyclic compound, a formulation resolved in the stomach or a formulation resolved in the intestine. Ueno '651 only describes a general formulation.

On the other hand, the present inventor found that more than 5% of the bicyclic tautomer is converted into the corresponding monocyclic tautomer under the condition of pH 2, and based on the findings, the inventor made the enteric coated composition of the present invention comprising the bicyclic compound, which is prevented from converting into its monocyclic tautomer in the stomach under the condition of pH 2 so that the bicyclic compound can be delivered to the intestine and act locally in the intestine.

Applicant submits that there is no information in cited reference to motivate a person skilled in the art to formulate the compounds recited in amended claim 1 such that the bicyclic compound is prevented from converting into its monocyclic tautomer in the stomach by covering with an enteric coating and to use the combination of the particular prostaglandin compounds recited in amended claim 1 and an enteric coating. Applicant submits that such combination is neither taught nor suggested by Ueno '651."

Applicant's arguments have been considered and were found persuasive based on the amendment to the claims. Accordingly, the 35 U.S.C. 102(e) rejection of claims 1 and 4 over Ueno et al. (EP 0979651) has been withdrawn.

- **Rejection under 35 U.S.C. §102(e) over Ueno (WO'912)**:

Applicant argued, "Applicant notes that Ueno '912 describes "Tablets or pills may be gastric or enteric-coated preparation" (see page 25, lines 12-13 of Ueno '912).

Applicant submits that Ueno '912 does not describe or suggest that nausea in the subject is effectively prevented by administering the specific bicyclic compound as an enteric coated formulation to a subject, and the bicyclic tautomer is well protected even under an acidic condition by providing said compound with an enteric coating (see page 20, lines 4-16 of the present application). In addition, Ueno '912 does not describe or suggest which is a more suitable formulation for the bicyclic compound, a formulation resolved in the stomach or a formulation resolved in the intestine. Ueno '912 only describes a general formulation.

On the other hand, the present inventor found that more than 5% of the bicyclic tautorner is converted into the corresponding monocyclic tautomer under the condition of pH 2, and based on the findings, the inventor made the enteric coated composition of the present invention comprising the bicyclic compound, which is prevented from converting into its monocyclic tautomer in the stomach under the condition of pH 2 so that the bicyclic compound can be delivered to the intestine and act locally in the intestine.

Applicant submits that there is no information in cited reference to motivate a person skilled in the art to formulate the compounds recited in amended claim 1 such that the bicyclic compound is prevented from converting into its monocyclic tautomer in the stomach by covering with an enteric coating and to use the combination of the particular prostaglandin compounds recited in amended claim 1 and an enteric coating. Applicant submits that such combination is neither taught nor suggested by Ueno '912."

Applicant's arguments have been considered and were found persuasive. Accordingly, the 35 U.S.C. 102(e) rejection of claims 1-19 over Ueno et al. (WO 03/030912) has been withdrawn. However, this rejection has now been reformulated as a 35 U.S.C. 103(a) rejection. Ueno '912 teaches teaches a prostaglandin compound as a chloride channel opener (Abstract). The composition is administered by oral administration (page 23, lines 10-19). Examples of solid compositions include tablets and pills that may be coated with an enteric coating or gastroenteric film (p. 25, lines 5-21). The formulas and compositions disclosed in instant claims 6-16, 18 and 19 are encompassed and disclosed by Ueno, who discloses various prostaglandin compounds of the present invention. With regards to the instant "enteric" coating, Ueno teaches that their "tablets or pills may be gastric or enteric-coated preparations" (page 25, lines 12-13). Ueno '912 is directed to enteric-coated preparations and thus is sufficient to meet the instant claims. One of ordinary skill in the art would be amply motivated to apply the enteric coatings of Ueno for release of drug (i.e., bicyclic compounds) into the intestines based on Ueno's teaching that enteric coatings can be employed. With regards to Applicant's limitations of new claims 20, 21, 24 and 25 that the "composition exhibits reduced nausea inducing effect than that of a composition without the enteric coating", it is the position of the Examiner that this limitation is met by Ueno. Ueno discloses the administration of enterically-coated tablets or pills. Thus, one of ordinary skill in the art would reasonably conclude that nausea would necessarily be prevented and/or that the nausea-induced effect would be reduced based on the incorporation of the enteric coating applied on the compound. With regards to Applicant's limitations of new claims 22, 23 and 26 for the specific enteric coatings, Ueno teaches that their "tablets or pills may be enteric-coated preparations" ([0060]). While the specific coatings are not

disclosed, one of ordinary skill in the art would employ any specific enteric coating, based on personal preference and/or the intended outcome. Ueno '912 is directed to enteric-coated preparations, whereby sustained release of the active ingredient is obtained; and thus, the particular enteric coating employed does not impart a patentable distinction over the teachings of Ueno, who explicitly recognizes and teaches use of enteric coatings. With regards to Applicant's limitations of new claims 27 and 28 of "for preventing irritation of the upper gastric organs" of instant claim 27 and of "for improving pharmaceutical effect of the bicyclic compound to the living body" of instant claim 28, these limitations are met by Ueno. Ueno, as delineated above, discloses the use of enteric coatings and thus, one of ordinary skill in the art would reasonably conclude that irritation of gastric organs would be reduced and/or eliminated based on the incorporation of the enteric coatings of Ueno. Ueno expressly teaches the use of enteric-coatings and consequently, would be effective in preventing irritation and/or nausea to a subject. Furthermore, the pharmaceutical effect of the bicylic compound would be improved based on the enteric coatings of Ueno, absent a showing of evidence to the contrary.

- **Rejection under 35 U.S.C. §103(a) over Ueno (US'174)**:

Applicant argued, "There is no disclosure of an enteric coating or enteric materials that may be compounded into the capsule base, either in the particular disclosure cited by the Examiner or elsewhere in the patent. Rather, Ueno '174 only generally discloses coatings and capsulating agents at col. 22, line 31, and Applicant submits that such a general disclosure does not teach or suggest the enteric requirement of the present invention in particular."

Applicant's arguments have been considered but were not found to be persuasive. It is noted that Ueno does not explicitly teach "enteric" coatings but rather teaches general "coatings" and "capsulating agents" at col. 22, line 31, as stated by Applicant. However the teaching of the generic "coatings and capsulating agents" by Ueno would encompass the species of "enteric" coatings claimed by Applicant. The general disclosure of "coatings and capsulating agents" by Ueno is therefore sufficient to read on the "enteric" coating claimed by Applicant. Ueno expressly teaches that coatings and capsulating agents can be employed in compositions intended for oral administration and as a result, would render obvious, the "enteric" coating feature recited herein by Applicant, as such coatings/capsulating agents would include "enteric" coatings. Hence, Applicant's arguments were not persuasive.

This rejection has been maintained herein.

- **Rejection under 35 U.S.C. §103(a) over Ueno (US'651)**:

Applicant argued, "Applicant notes that Ueno '651 describes "Tablets or pills may be gastric or enteric-coated preparation" (see [0060] of Ueno '651). Applicant submits that Ueno '651 does not describe or suggest that nausea in the subject is effectively prevented by administering the specific bicyclic compound as an enteric coated formulation to a subject, and the bicyclic tautomer is well protected even under an acidic condition by providing said compound with an enteric coating (see page 20, lines 4-16 of the present application). In addition, Ueno '651 does not describe or suggest which is a more suitable formulation for the bicyclic compound, a formulation resolved in the stomach or a formulation resolved in the intestine. Ueno '651 only describes a general formulation.

On the other hand, the present inventor found that more than 5% of the bicyclic tautorner is converted into the corresponding monocyclic tautomer under the condition of pH 2, and based on the findings, the inventor made the enteric coated composition of the present invention comprising the bicyclic compound, which is prevented from converting into its monocyclic

tautomer in the stomach under the condition of pH 2 so that the bicyclic compound can be delivered to the intestine and act locally in the intestine.

Applicant submits that there is no information in cited reference to motivate a person skilled in the art to formulate the compounds recited in amended claim 1 such that the bicyclic compound is prevented from converting into its monocyclic tautomer in the stomach by covering with an enteric coating and to use the combination of the particular prostaglandin compounds recited in amended claim 1 and an enteric coating. Applicant submits that such combination is neither taught nor suggested by Ueno '651."

Applicant's arguments have been considered but were not deemed persuasive. As stated by Applicant, Ueno teaches that their "tablets or pills may be gastric or enteric-coated preparations" ([0060]). Thus, Applicant's argument that "Ueno '651 does not describe or suggest which is a more suitable formulation for the bicyclic compound, a formulation resolved in the stomach or a formulation resolved in the intestine" was not persuasive since Ueno '651 specifically teaches that "tablets or pills may be enteric coated". The argument that "there is no information in cited reference to motivate a person skilled in the art to formulate the compounds recited in amended claim 1 such that the bicyclic compound is prevented from converting into its monocyclic tautomer in the stomach by covering with an enteric coating" was not persuasive, since as delineated above, Ueno '651 is directed to enteric-coated preparations and thus is sufficient to meet the instant claims. One of ordinary skill in the art would be amply motivated to apply the enteric coatings of Ueno for release of drug (i.e., bicyclic compounds) into the intestines based on Ueno's teaching that enteric coatings can be employed. Applicant's argument that "Ueno '651 does not describe or suggest that nausea in the subject is effectively prevented by administering the specific bicyclic compound as an enteric coated formulation to a subject, and the bicyclic tautomer is well protected even under an acidic

condition by providing said compound with an enteric coating" was not persuasive. As noted above, Ueno teaches the administration of enterically-coated tablets or pills. Thus, one of ordinary skill in the art would reasonably conclude that nausea would necessarily be prevented based on the incorporation of the enteric coating applied on the compound. Furthermore, note that the claim (i.e., instant claim 27) recites "for preventing irritation of the upper gastric organs" and not "for preventing nausea" as argued by Applicant. Nonetheless, Ueno expressly teaches the use of enteric-coatings and consequently, would be effective in preventing irritation and/or nausea to a subject. Hence, Applicant's arguments were not held persuasive.

This rejection has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

-- No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

January 3, 2011